



**Structure of RGL3 and alignment of RasGEF, RasGEF and RA motifs.**

**FIG. 1A**  
RGL3 (710 a.a.)



Annotated Sheet Showing Changes  
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**FIG. 1**

**FIG. 1B**  
**RasGEFN motif**

	10	20	30	40	50	60
consensus	...*... .....*	..... .....*	..... .....*	..... .....*	..... .....*	..... .....*
RGL3	1 CKGGLIKGGTLEKLIIEHLTEARDK-VDPFTFVETFLTYRSFITTQELLIQKLLYRNYAIPP 59					
gi 1354501	64 SKVRLVRAARLERLVLGELVFGDRE-QDPSFMPAFLATYRTFVPTACLLGFLLP--PMPPP 120					
gi 158471	87 RSSRRLRAGTLEALVRHILLDARTagADMMFTPALLAHTRAFTSTPALEGLVADRLEALES 146					
gi 544403	636 AGVPMIKGATLCKLIERLTYHLY--ADPTFVVRTFILTTYRYFCSPQQLIQLLVERFNI PDP 693					
	111 CKVRTVKAGTLEKLVLEHLVPAFQg-SDLSSYVTVFLCTYRAFTTTQQVLDLFFKRYGCILP 169					
consensus	70 ..*... .....*	80 ..*... .....*	90 ..*... .....*	100 ..*... .....*	110 ..*... .....*	120 ..*... .....*
RGL3	60 EGVE-----D-----IWWKEKVNPRRIQ---NRVLNILRLWV 88					
gi 1354501	121 PPPG-----V-----EIRKTAVQDLTSFNkn1RAVVSVLSWSWL 152					
gi 158471	147 Y-----PPGELERTT---GVAISVLSSTWL 167					
gi 544403	694 SLVYqdtgtagggmggggDkenknshredwkrYRKEYVQP--VQ---FRVLNVLRHWV 748					
	170 YSS-----eDg-----GPQDQLK---NAISSILGTWL 193					
consensus	130 ..*... .....*	140 ..*... .....*	150 ..*... .....*	160 ..*... .....*		
RGL3	89 ENYWQDFEEDPKLNLFLEE-FLELVDDK-KYPGLETSLQNILLRRLS 132 SEQ ID NO: 54					
gi 1354501	153 QDHPOQDFRDHPahsd1gsvrtflgwaapgsaeaqkaek11edf1ee 198 SEQ ID NO: 55					
gi 158471	168 ASHPEDFGSEVKGQQLDRLE-SFLLRTGYAAREGVVGGSAIDLIRNLR 212 SEQ ID NO: 56					
gi 544403	749 DHHFYDFEKDPMLLEKLLN-FLEHVNGK-SMRKWDVSVLKIVQRKN 792 SEQ ID NO: 57					
	194 DQYSEDFCQP-PDFPCLKQ1VAYVQLNM-PGSDLERRAHLLAQLE 237 SEQ ID NO: 58					



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**FIG. 1**

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FIG. 1

**FIG. 1C**  
**RasGEF motif**

	10	20	30	40	50	60
consensus	1	LLLDPKELAEQLTLLDFELLRKIDPSELLGSVWGRSKKS--PSPL--NLERTIERFNE	56			
RGL3	243	LLDFSVDEVAEQLTLIDLEFSKVRLYECLGSVWSQDRPGaaGASP--TVRATVAQFNT	300			
1BKD_S	171	LLLHPIELARQLTLESIDLRAVQPSSELVGSVWTKEDKEI--NSP--NLLKMRIRHTTN	225			
gi 544403	363	LLFPPDILVAEQFTLMDAELFKVVKVPSQRAKRG--KEH1aptIRATVAQFNM	420			
gi 6919956	239	VLVFLADHILAEQLTLLDAELFLNLIPSQCLGGIWLGHDRRPG--HSH1cpSVRATVTFQFNK	296			
	70	80	90	100	110	120
consensus	57	VSNWVATEILKQTT-----P--KDRAEILSKFIFIQVAKHCRELNNFNSLMAI	100			
RGL3	301	VTGCVLGSVLGAPG-----LaapQRAQRLEKWIIRIAQRCRELRFNSSSLRAI	346			
1BKD_S	226	LTLWFEKCIIVETEN-----L--EERVAVVSRRIIEILQVFQELNNFNGVLEV	269			
gi 544403	421	VANCVITTCLGDSm-----KA--SDRARVVEHWIEVAARECRLVKNFSSLYAI	466			
gi 6919956	297	VAGAVVSSVVLGATstgegpgevtirplrp--PQRARLLEKWIIRVAECRLLRNFSVVYAV	354			
	130	140	150	160	170	180
consensus	101	VSALSSSPISRLKKTWEKLP SKYKKLFEELLELDPSRNFKNYREALISSCN-----	151			
RGL3	347	LSALQSNPIYRLKRSWGAVERPLSTERKLSQLFISDENNHILSSREILFQEEategsseed	406			
1BKD_S	270	VSAMNNSSPVYRLDHTFEQIPSRSQKKILEEAHLSSE--DHYKKYLAKLRSIN-----	318			
gi 544403	467	LSALQSNAIHLKKTWEVSRGSFDRVQKLSEIFSDDNNYSLSRELLIKEGtksfatlem	526			
gi 6919956	355	VSALQSSPIHLRAWGEATRDSLRFSSLQCIFSeedNYSQSRELLVQEVk1qspleh	414			
	190	200	210	220	230	240
consensus	152	-----LPPCIPFLGVLLKDLTFIDEGNPDFLKN--GLVNFEKRRKIAKIL	194			
RGL3	407	n-----tpgslpskppPGPVYLGTFFLTDLVMLDLKTTEEGNPEVLKRhgkELINFSKRRKVAEIT	459			
1BKD_S	319	-----PPCVPFFFGIGYLNTNLKTEEGNPEVLKRhgkELINFSKRRKVAEIT	363			
gi 544403	527	nprrtqrrqketgviiQGTVPYLGTFFLTDLVMLDTAMKDLYG--RLINFEKRRKEFEV	583			
gi 6919956	415	s----kkaprsgrggVVVYLGTFFLKDLVMLDAASKDELEN---GYINFDFKRRKEFAVL	467			

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**FIG. 1C**

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**FIG. 1C**  
**RasGEF motif**  
(Continued)

	250	260	270	280	290
	*	*	*	*	*
consensus	195	REIRQLQS--QPYNLRPNSRDIQSSLQQS--LDSLPEEN--ELYELSLRIEPRV	242	SEQ ID NO: 59	
RGL3	460	ARIQQQLQRRcQSYTLLSPHPPIAAL--HA--QNQLTTEEQ---SYRLSRVTEPPa	506	SEQ ID NO: 60	
1BKD_S	364	GEIQQYQN--QPYCLRVE--SDIKRFFENLmpGMGNSMEKEftdyLFNKSLEIEPRN	415	SEQ ID NO: 61	
gi_544403	584	AQIKLLQSacNNYStVPE-EHFGAWFRAM---GRLSEA---ESYNLSCLEPPS	630	SEQ ID NO: 62	
gi_6919956	468	SELRRLQNEcRGYNLQPD-HDIQRWLQG---LRPLTEA---QSHRVScVEPPG	514	SEQ ID NO: 63	

**FIG. 1D**  
**RA motif**

	10	20	30	40	50	60
	*	*	*	*	*	*
consensus	1	DQGVLRVYFQDLKPGVAYKTIRVSSEDTAPDVVQLALEKFRRLDDEDPEEYALVEVLSGDK	60			
RGL3	613	earVTRVSIDNDH-GNLYRSILLTSQDKAPSIVVRRALQKHNVFQPWACDYQLFQVLPGDR	671			
1EF5_A	17	DTCIIRISVEDn-NGNMVKSIIMLTSQDKTPEAVIQRAMSKHNLESDPAEEYELVQVISEDK	75			
1RLF	4	DCRIIRVQMLEgedGSVYKSLIVTSQDKAFSVISRVLKKNNRDSAVASEFELVQLLPGDR	63			
1LXD_A	15	DCCIIRVSLDVD-NGNMVKSLVTSQDKAPTVKAMDKNLDEDEPEDYELLQIISEDH	73			
	70	80	90			
	*	*	*	*	*	*
consensus	61	ERKLPPDENPLQLRLLNIPRDGLSLRFLLKRRD	92	SEQ ID NO: 64		
RGL3	672	VLLIPDNANVFYAM--SPVAPRDFMLRRKE	699	SEQ ID NO: 65		
1EF5_A	76	ELV1PDSANVFYAMNSQVN---FDFLILRKKN	103	SEQ ID NO: 66		
1RLF	64	ELTIPHSANVFYAMDGAS---HDFLLRQRR	90	SEQ ID NO: 67		
1LXD_A	74	KLKIPENANVFYAMNSAAN---YDFILLKRR-	100	SEQ ID NO: 68		

**FIG. 1**

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**FIG. 1**

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**Structure of RGL3 and alignment of RasGEF, RasGEF and RA motifs.**

**FIG. 1A**

RGL3 (710 a.a.)



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**FIG. 1B**  
**RasGEF/N motif**

	10	20	30	40	50	60	
consensus	1 CKGGLIKGGTLEKLIIEHLTEARDK-VDPPTFVETFLTYRSFITTQELLQKLLYRYNAPIPP	59					
RGL3	64 SKVRVLRAARLERLVGELVFGDRE-QDPSFMPAFLATYRTFVPTACLLGFLLP--PMPPP	120					
gi 1354501	87 RSSRRLRAGTLEALVRHLLDARTagADMMPFTPALIATHRAFTSTPALFGLYVADRLEALES	146					
gi 158471	636 AGVPMIKGATLCKLIERLTYHIY--ADPTFVRTFLFTTYRYFCSPQQQLLVERFNIPDP	693					
gi 544403	111 CKVRTVKAGGLEKLVEHLLVPAFQg-SDLSYVTVFLCTYRAFTTTQQVLDLLFKRYGCILP	169					
	70	80	90	100	110	120	
consensus	60 EGVED-----D-----V-----V-----						
RGL3	121 PPPG-----V-----V-----eDg-----						
gi 1354501	147 Y-----						
gi 158471	694 SIVyyqdttagaggmgggDkehknshredwkyRKEYVQP--VQ--						
gi 544403	170 Yss-----						
	130	140	150	160			
consensus	89 ENYwQDFFEDPKLNLFLEE-FLELVDDK-KYPGLETSLQNILLRRLS	132	SEQ ID NO: 54				
RGL3	153 QDHQDFFRDPahsdlgsvrflgwaapgsaeaqkaek11edflee	198	SEQ ID NO: 55				
gi 1354501	168 ASHPEDFGSEVKGQLDRLE-SFLLRRTGYaAREGVVGGSAIDLIRNLR	212	SEQ ID NO: 56				
gi 158471	749 DHHFYDFEKDPMLLEKLLN-FLEHVNGK-SMRKwVDSVLKIVQRKN	792	SEQ ID NO: 57				
gi 544403	194 DQYSEDFCQP-PDFFPCLKQ1VAYVQLNM-PGSDLERRAHLLIAQLE	237	SEQ ID NO: 58				

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**FIG. 1C**  
**RasGEF motif**

	10	20	30	40	50	60
	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*
consensus	1 LLLDPKELAEQLTILLDFELFRKIDPSELLGSGVWGKRSKKSS--PSPL--NLERFIERFNE	56				
RGL3	243 LIDFSVDEVAEQLTILDLF SKVRLYECIGSVWWSQRDRPGaaGASP--TVRATVAQFNT	300				
1BKD_S	171 LITLHPIETIARQLTILLESDLYRAVQPSELGVGSWMTKEDKEI--NSP---NLLKMRIRHTTN	225				
gi 544403	363 LLLFPFDLVAEQFTLMDAELFRKKVVPYHCLGSIMSQRAKKG--KEHIaptIRATVAQFNN	420				
gi 6919956	239 VLVFLADHIAEQLTLLDAELFLNLIPSCQLGGIwGHRDRPG--HSH1cPSVRATVTQFNK	296				
	70	80	90	100	110	120
	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*
consensus	57 VSNWVATEILKQTT-----P--KDRAEILSKFIQVAKHCRELNFFNSLMAI	100				
RGL3	301 VIGCIGVLSVLGAPG-----LaaPQRQAQRLEKWMIRIAQRCRELNFSSLRAI	346				
1BKD_S	226 LTLWFEKCIIVETEN-----L--EERVAVVSRILIEILQVFQELNNFNGVLEV	269				
gi 544403	421 VANCVITTCGLDQSm-----ka--SDRARVVEHMIIEVARCRLVKNFSSLYAI	466				
gi 6919956	297 VAGAVVSSVLGATSTgegpgtgtirplP--PQRARLLEKWMIRVAEECRLLRNFSVVYAV	354				
	130	140	150	160	170	180
	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*
consensus	101 VSALSSSSPISRILKKTWEKLPSKYKKLFFEEELDFPSRNFKNYREALSSCN-----	151				
RGL3	347 LSALQSNPPIYRLKRSWGAWSREPLSTFRKLSQIFSDENNHLSREILFQEEatgsqeed	406				
1BKD_S	270 VSAMNSSSPVYRLDDHTFEQIPIRSRQKKLILEEAHELSE--DHYKKYLAKLRSIN-----	318				
gi 544403	467 LSALQSNAIHRLKKTWEEVSRGSFRVFKLSEIFSDenNYSLSRELLIKEGtkskfatlem	526				
gi 6919956	355 VSALQSSPIIHLRAAMGEATRDSLRFVSSLQCIFSeedNYSQSRELLVQEVk1qspleh	414				
	190	200	210	220	230	240
	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*	.....*..... .....*
consensus	152 -----LPPCIPFLGVLLKDLTFIDEGNPDLFLKN---GLVNFEKRRKIAKIL	194				
RGL3	407 n-----tpgs1pskppPGPVPYLTGTFLTDLVMLDTALPDMLEG--DLINFEKRRKEWEIL	459				
1BKD_S	319 -----PPCVPPFFGIGYLTNILKTEEGNPEVLKRhgkELINFSKRKVAEIT	363				
gi 544403	527 nprrtqrrqketgv1QGTVPYLYGTFLTDLVMLDTAMKDLYG--RLINFEKRRKEFEV1	583				
gi 6919956	415 s----kkaprgsrgGGVVPPYLGTFLKDLVMLDAASKDEL---GYINFDKRKEFAVL	477				

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**FIG. 1C**  
**RasGEF motif**  
(Continued)

	250	260	270	280	290
consensus	195 RETRQLQS--QPYNLRPNRSDIQSLLQQS--LDSLPEEN---ELYELSLRIEPRV	242	SEQ ID NO: 59		
RGL3	460 ARIQQLQRrcQSYTLSPHPPILAA--HA--QNQLTTEQ---SYRLSRVIEPPa	506	SEQ ID NO: 60		
1BKD_S	364 GEIQQYQN--QPYCLRVE-SDIKRFFENlpGMGNSMEKEft-dYLFNKSLEIEPRN	415	SEQ ID NO: 61		
gi 544403	584 AQIKLLQSacNNYStVPE-EHFGAWFRAM---GRLSEA---ESYNLSCLEPPS	630	SEQ ID NO: 62		
gi 6919956	468 SELRRQEcRGYNLQPD-HDIQRWLQG---LRPLTEA---QSHRVSCEVEPPG	514	SEQ ID NO: 63		

**FIG. 1D**  
**RA motif**

	10	20	30	40	50	60
consensus	1 DQGVLRVYFQDLKPGVAYKTIRVSSEDTAFDVVQLALEKFRLLDDDEDPEEYALVEVLSGDK	60				
RGL3	613 earVTRVSIDNDH-GNLYRSILLTSQDKAPSVRRAQKHNVPQWACDYQLFQVLPGDR	671				
1EF5_A	17 DTCIIRISVEDn-NGNMYSKISIMLTSQDKTPAVIQRAMSKHNLSEDAEYELYQVISEDK	75				
1RLF	4 DCRIIRVQMLELgedGSVYKSLVTSQDKAPSVISRVLKNNRDSAVASEFELVQLLPGDR	63				
1LXD_A	15 DCCCIIRVSLDVD-NGNMYSKISILVTSQDKAPTVIRKAMDKHNLDEDEPEDYELLQIISEDH	73				
		70	80	90		
consensus	61 ERKLPPDENPLQLRLNLPRDGLSLRFLLKRRD	92	SEQ ID NO: 64			
RGL3	672 VLLIPDNANVFYAM---SPVAPRDFMLRKE	699	SEQ ID NO: 65			
1EF5_A	76 ELVIPDSANVFYAMNSQVN---EDFILRKNN	103	SEQ ID NO: 66			
1RLF	64 ELTIPHSANVFYAMDGAS---HDFLLRQRR	90	SEQ ID NO: 67			
1LXD_A	74 RLKIPENANVFYAMNSAAN---YDFILKKR-	100	SEQ ID NO: 68			

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